REMARKS

This paper is filed in response to the Office Action, mailed June 17, 2004. A response to the Office Action was due on September 17, 2004. Applicant is filing this response with a three-month extension of time, therefore, this response, filed on or before December 17, 2004, is to be considered timely.

Claims 1-26 are pending in the application. Claims 1-26 have been rejected. Claim 25 has been objected to. Applicant has amended claim 25. No new subject matter has been added to the subject application with the filing of this preliminary amendment. Applicants reserve their right to file continuation applications on the subject matter from the canceled claims.

Information Disclosure Statement

Applicant acknowledges the Examiner's receipt of the IDS and wishes to thank the Examiner for the acknowledgment of the applicant's references via the initialed PTO-1449.

Trademarks and Specification

The Examiner stated that applicant's use of trademarks in the application have been noted and per the Examiner's suggestion, the terms on page 3, lines 1-5 and page 6, lines 11-16 have been amended so that they are now capitalized and accompanied by the appropriate generic terminology. The basis for this amendment is that one of ordinary skill in the art could reference a standard reference volume, i.e. Physician's Desk Reference, and derive the generic names from the trademarked brand names.

Claim Objections

The Examiner stated that claim 25 has been objected to, due to a lack of a period at the end of line 2. In response, applicant has amended claim 25 to correct this typo.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner stated that claims 1-26 were rejected under §112, first paragraph, because the specification, while being enabling for the treatment of

neuoroblastoma, glioblastoma and rhabdomyosarcoma, does not reasonably provide enablement for the treatment of all types cancer using the claimed compounds. In support of this position, the Examiner cited **In re Wands**, 8 USPQ2d 1400 (Fed. Cir. 1988). Applicant respectfully traverses this rejection and provides the following comments.

In response, applicant respectfully states that per the **Wands** factors, that applicant has enabled the claims to treat cancer. With regard to the state of prior art, applicant respectfully notes that the general knowledge in the art recognizes the utility of temozolomide and irinotecan for numerous types of cancers (see generally cited art on first page of applicants specification). Further, while the Examiner points out specific references stating that these compounds are effective against certain types of cancers, applicant respectfully points that even the Burton reference cited by the Examiner notes that temozolomide acts generally with an anti-tumor effect by methylation of tumor DNA, while irinotecan acts by inhibiting topoisomerase I, an enzyme that normally functions to relieve torsional strain caused by the synthesis of new strands of DNA or RNA around a double helix (see Burton, page 3, middle two paragraphs). Applicant respectfully suggests that cancers other than those specified by the Examiner can be treated by these compounds due to general cytotoxic chemotherapeutic action they inflict on tumor DNA. Therefore, these compounds are enabled by the art and the specification to treat cancer. In support of this, applicants refer the Examiner to the references cited on page 1 of the specification. Copies of these references have been provided to the Examiner in an IDS filed on May 21, 2003. Applicant suggests that the examples provided in the specification on pages 7-24, in addition to the general knowledge in the art, provide a sufficient road map to one of ordinary skill in the art to prevent anyone from being unduly burdened from experimenting with the claimed invention.

Thus contrary to the Examiner's rejection, applicants suggest that the combination of the two compounds, as claimed herein are enabled to treat cancer and therefore, applicants respectfully request the withdrawal of this rejection.

Rejection under 35 U.S.C. §103(a)

Claims 1-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the WO 97/12630 in view of Ragab U.S. 6,346,524 and Burton et al. The Examiner stated that Burton et al. discuss new chemotherapy options for patients suffering gliomas, in particular the use of temozolomide and irinotecan. The Examiner stated that single dosing of temozolomide and irinotecan had been demonstrated by Burton be effective in certain cancer treatments. The Examiner stated that Ragab demonstrated administering an effective amount (40-150 mg/m^2/day) for a dosing period of from about 5 to 25 days to cure or eliminate cancer. The Examiner cited **In re Susi**, 169 USPQ 423, 426 (CCPA 1971); **In re Kerkhoven**, 205 USPQ 1069 (CCPA 1980) for the premise that it is prima facie obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose." Additionally, Claim 26, drawn to a medical kit, was also rejected under §103.

Applicants respectfully traverse the rejection and provide the following comments.

Per Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966) and MPEP § 2144, the criteria for a prima facie case of obviousness are:

- Determining the scope and contents of the prior art.
- Ascertaining the differences between the prior art and the claims at issue.
- Resolving the level of ordinary skill in the pertinent art.
- Considering objective evidence in the application indicating obviousness or nonobviousness.

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a prima facie case of obviousness. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The Examiner can satisfy this burden only by showing an objective teaching in the prior art, or knowledge generally available to one of ordinary skill in the art, which would lead an individual to combine the relevant teachings of the references [and/or the knowledge] in the manner suggested by the Examiner. Id.; In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d at 1784; In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989); In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

"It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious....'[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.'" In re Fritch, 23 U.S.P.Q.2d at 1784 (quoting In re Fine, 5 U.S.P.Q.2d at 1600).

Because of the differences between the scope of the prior art and the claimed invention, per the first and second Graham factors, applicant respectfully suggests that a prima facie case of obviousness cannot be established.

Applicant claims a method of treatment using therapeutically effective amounts of temozolomide in combination with irinotecan. Therapeutically effective amounts temozolomide and irinotecan are described on pages 4-6 of the specification. Applicant notes that the Examiner concedes that neither reference teaches a combination of temozolomide and irinotecan.

The Examiner references Ragab and Burton et al. for their disclosure of temozolomide and irinotecan. However, there is no teaching or suggestion in either reference to combine irinotecan in combination with temozolomide to treat cancer.

In fact, Burton et al. teaches away from the applicant's invention by the fact that it mentions both monotherapy with irinotecan AND temozolomide, but as the Examiner concedes, does not teach a combination therapy of the two compounds. Further, Ragab merely discloses the use of temozolomide **alone**, (see generally, Abstract, col. 2, lines 31-45 and claims 1-11 of Ragab) there is no teaching or suggestion of combination therapy with irinotecan. In addition, applicant believes that one of ordinary skill in the art would not necessarily consider Ragab's mono therapy of temozolomide to treat cancer when practicing the combination temozolomide and irinotecan therapy described by the applicant's invention. Finally, neither Ragab or Burton et al. contain any teaching or suggestion to combine any of them in order to teach applicant's claimed invention, temozolomide

in combination with irinotecan. Applicant respectfully suggests that per the first and second Graham factors, these differences in the scope and contents of the claimed invention from the cited art preclude a finding of obviousness.

Lastly, with regard to the Examiner's citation of **In re Susi**, 169 USPQ 423, 426 (CCPA 1971); **In re Kerkhoven**, 205 USPQ 1069 (CCPA 1980), applicant respectfully points out that neither case is relevant to the applicant's invention for the following reason. **Susi** dealt with a method of stabilizing a polymer against UV light based on the combination of known stabilizers. 169 USPQ 423 at 426. **Kerkhoven** dealt with a method of mixing ionic and anionic detergents together in an effort to form a combined detergent composition. 205 USPQ at 1069-1071. Applicant respectfully points that neither case is applicable to this case because of the unique challenges in combination therapy to treat disease, versus merely trying to increase the stabilization of polymers or the simple admixture of two individual detergents to form an improved combination detergent. The language quoted by the Examiner notes that the **combining** of "two compositions. . . useful for the same purpose, in order to **form** a third composition" would be prima facie obvious. However, applicant DOES NOT combine two compositions to form a third composition, rather it is the administration of two compounds, one by oral administration (temodar) and one intravenously (irinotecan), into a patient for treatment of a disease. Unlike the case law cited by the Examiner, there is no combination of compounds to form a third compound.

Furthermore, the efficacy of a drug with respect to a particular disease cannot be predicted based upon treatment of that disease with a structurally and functionally distinct drug, such as irinotecan and temozolomide. Thus, one having ordinary skill in the art could not predict for irinotecan whether the total drug exposure or its peak plasma level would be important in treating cancer because temozolomide and irinotecan are different drugs. Thus, the references cited by the Examiner are not predictive of treating cancer with irinotecan and temozolomide, especially due to the synergistic effects stated by the specification by Example C, starting on page 7, line 20 to page 10, line 23.

Therefore, applicant respectfully submits that the claimed invention is not obvious in light of Ragab and Burton et al. Reconsideration and withdrawal of this ground of rejection is respectfully urged.

In view of the remarks above, applicant respectfully submits that the application is in condition for allowance. Accordingly, applicant requests reconsideration of the application, withdrawal of the rejections of record and issuance of a Notice of Allowance.

No fees, other than the appropriate extension of time fees, are due by the submission of this paper however, if any fees are determined to be due by this paper, the Commissioner is hereby authorized to deduct such fees from **Account No. 19-0365.**

The Examiner is requested to call the undersigned attorney on any matter connected with this application.

Respectfully submitted,

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